Organization: University of Washington

Title: Molecular Engineering of Surfaces for Sensing and Detection

MTO **Simbiosys**

Start Date: June 2001 **End Date:** June 2004

Principal Investigator(s): Shaoyi Jiang
Phone: (206) 616-6510 Email: sjiang@u.washington.edu
Web: http://depts.washington.edu/~chemeng/faculty/jiang.html

Agent: Tom Renz AFRL (315) 330-3423 renzt@rl.af.mil

Project Goals

The goals of this project are to (1) predict protein orientation on surfaces using hierarchy simulation approaches, (2) control and manipulate complex microenvironments on surfaces at the molecular level for the oriented immobilization of proteins, and (3) develop a surface analytical technique to detect protein orientation. The success of simulation work will provide a tool to predict protein orientation and to rationally design a surface for the oriented immobilization of proteins. Experimental activities will develop innovative methods to control and manipulate surface properties for the molecular recognition of proteins and to detect protein orientation on surfaces. Surface engineering at the molecular level will maximize the sensitivity and specificity of bio-molecular microsystems for sensing and detection.

Technical Approach

- The adsorbed amount, orientation, and conformation of antibody molecules on surfaces will be controlled and manipulated by adjusting microenvironments (e.g., nano-scale chemical and structural surface properties and solution properties).
- Monte Carlo (MC) simulations with a 12-bead model will be used to qualitatively predict protein orientation on surfaces while MC simulations with a residue-based model will provide quantitative prediction of antibody orientation of a specific protein on surfaces. For the quantitative prediction of protein conformation on surfaces, Brownian dynamics (BD) or molecular dynamics (MD) simulations with an all-atom model are needed. The cell-multipole method and massively parallel computing technique will be incorporated to accelerate all-atom simulations.
- Surface plasmon resonance (SPR) biosensors will be used to study the interactions between antigens and antibodies immobilized on functionalized surfaces (e.g., mixed -COOH, -NH2, and -OH terminated thiols). SPR results will provide some information regarding antibody orientation. The direct information of antibody orientation will be obtained by time-of-flight secondary ion mass spectrometry (ToF-SIMS).
- The integrated computational and experimental approach will enable the study of molecular events occurring at the interfaces between biological media and man-made surfaces in a way never attempted before.

Recent Accomplishments

- Predicted antibody orientation on surfaces under various conditions from MC simulations based on a 12-bead model and developed a residue-based model for protein simulations.
- Validated the hypothesis that antibody orientation can be controlled by varying microenvironments by SPR and initiated the work to control adsorbed proteins on surfaces using an electrochemical method.
- Applied ToF-SIMS for the detection of antibody orientation on surfaces for the first time.

Six-Month Milestones

- Complete the residue-based model for protein simulations and continue to develop a computer program for Brownian simulations of protein interactions with surfaces based on an all-atom model.
- Provide further experimental evidence for the manipulation of antibody orientation and optimize conditions for the oriented immobilization of antibody molecules on surfaces
- Complete the work on the detection of antibody orientation using ToF-SIMS.

Team Member Organizations

N/A

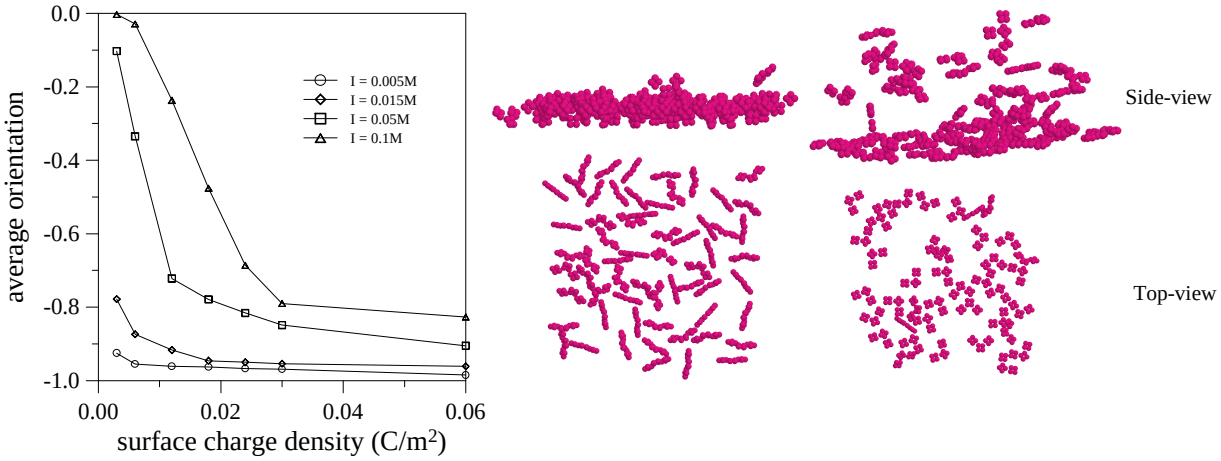

Figure 1. Effects of surface charge density and ionic strength on antibody orientation, where "–1" indicates "end-one" orientation (left) and snapshots of 12 beads antibody configuration on surface (right).

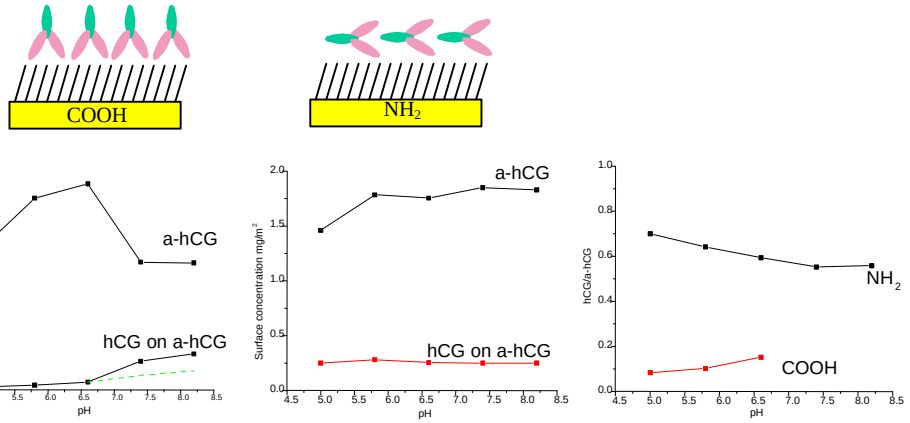

Figure 2. Antibody adsorption and its immuno reaction to antigen on negatively (left) and positively (center) charged surfaces and the ratio of antigen to antibody on different surfaces (right) by SPR.

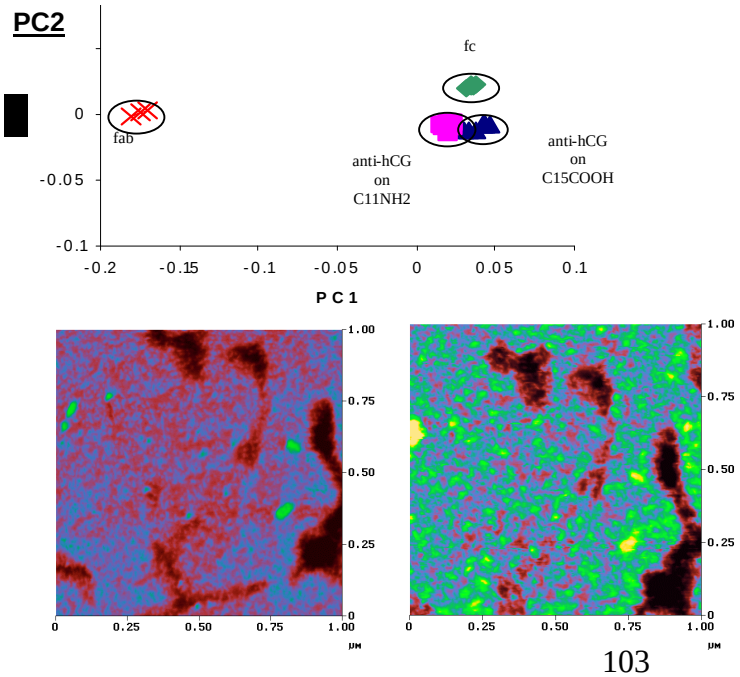

Figure 3. Probing surface immobilized antibody orientation by applying principal component analysis to ToF-SIMS spectra

Figure 4. In-situ tapping-mode AFM images of hCG and anti-hCG interactions for immobilized hCG (left) and after anti-hCG injection (right). Blue, green, red and dark red represent hCG, anti-hCG, substrate and defects on Au (111).